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EXAMINER

LAMBERTSON, DAVID A

ART UNIT	PAPER NUMBER
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1636

DATE MAILED: 02/25/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

10/009,178

Applicant(s)

OKAMOTO, HIROSHI

Examiner

David A. Lambertson

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 02 December 2003.
- 2a) ☐ This action is FINAL. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-19 is/are pending in the application.
- 4a) Of the above claim(s) 2,6,8-13,17 and 19 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1,3-5,7,14-16 and 18 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☒ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All b) ☐ Some * c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☐ Certified copies of the priority documents have been received in Application No. _____.
 - ☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftperson's Patent Drawing Review (PTO-948)
- 3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date _____
- 4) ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date _____
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: _____

DETAILED ACTION***Election/Restrictions***

Applicant's election with traverse of Group I (Claims 1, 3-5, 7 and 14-16; newly presented claim 18 is now entered into this group) in the response filed December 2, 2003 is acknowledged. The traversal is on the ground(s) that unity exists between all of the claimed inventions for several reasons. Applicant argues:

1. That there is a special technical feature between the claimed nucleic acids and the claimed protein/peptides because, as set forth in example 17 of Annex B, Part II of Appendix AI in the MPEP, exemplary claims reading "a protein X" and a DNA sequence encoding protein X" are accepted as having unity.
2. There is not an undue search burden on the Office as it pertains to the examination of the nucleic acids and proteins as claimed in the instant application.
3. Applicant asserts that the different methods as set forth in claims 8, 9, 11 and 12 share the same special technical feature in that they use the novel proteins of SEQ ID NO: 2 or SEQ ID NO: 4, and that the steps for all of the methods are "quite similar and overlap each other."
4. Furthermore, Applicant argues that the only difference between the methods claimed in claims 9 and 11 is that the use of an isolated molecule versus a molecule present on a cell surface.

Based on these arguments, Applicant requests that all claims be examined together in this single application.

This is not found persuasive because of the following reasons:

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1. Applicants interpretation that the example set forth in example 17 of Annex B, Part II of Appendix AI in the MPEP pertains to the instant claims is not persuasive. The example pertains to unity of invention existing between a nucleic acid and a protein when there is a direct correspondence between a DNA sequence encoding a specific protein sequence, and the specific protein encoded by the specific DNA sequence. However, the instant claims refer to variations in the protein sequences that are claimed, including any addition, deletion, substitution or insertion of amino acids, and thus do not contain such a direct correspondence.

In order for there to be unity of invention, there must be a special technical feature that links the inventions. With regard to a linking technical feature between a DNA sequence and an amino acid sequence, this feature must be a one-to-one correspondence between the two sequences (i.e., the DNA must necessarily encode the protein, and the protein must necessarily be encoded by the DNA). This is clearly evident from the example in example 17 of Annex B, Part II of Appendix AI in the MPEP, cited by applicant, because there is no indication that variants of nucleic acid or amino acid sequences retain a special technical feature. Additionally, it is noted that SEQ ID NO: 1 and 3 *are not* coding sequences, and contain nucleic acids that do not correspond to the protein sequences that are claimed; again, this disrupts the concept that the nucleic acid sequence encodes the protein on a one-to-one correspondence, thereby representing a special technical feature.

In the instant case, there is an absence of the required one-to-one correspondence between the claimed nucleic acid and amino acid sequences, thus there is no linking special technical feature. This is evident in sections (c) and (g) of claim 1, where the

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DNA encodes “variant proteins” (i.e., proteins where amino acids that represent the special technical feature of the protein can be altered by addition, insertion, deletion or substitution). The fact that the amino acid sequence is changed requires that the nucleic acid sequence be changed; therefore the special technical feature between the claimed NDA and protein sequences is broken. Additionally, there is no one-to-one correspondence between the nucleic acid and amino acid sequences because the nucleic acid contains *non-coding* sequences. As such, the restriction of the instant claims as having different special technical features is not in error under the practice of unity of invention, as applicant purports.

2. The burden of search is present, despite Applicant’s assertion to the contrary. In order to search the separate sequences (nucleic acid and protein), separate searches or different databases would be required because a search of the nucleic acid sequences would not reveal protein sequences. This is especially true in light of the fact that the DNA sequences contain non-coding sequences. Therefore, because the searches are not co-extensive, a search of both inventions would be unduly burdensome.

3 and 4. Applicant’s arguments as they regard the rejoinder of Groups VII-X are moot in relation to the instant invention, and the restriction under practice of lack of unity. When establishing a lack of unity, the special technical feature of all groups/claims is only considered with respect to the special technical feature of the first group (i.e., Group I). Applicant wishes to consider the special technical features between groups that do not relate back to Group I, i.e., the special technical feature of Groups VII-X. However, there are no arguments to indicate that there is a special technical feature that is shared between Group I and Groups VII-X. Therefore, Groups VII-X will not be rejoined to

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Group I based on the instant arguments. Furthermore, since lack of unity practice will not be employed in future applications (since those applications will not be filed under 35 USC 371) regarding the restriction of Groups VII-X, the special technical features of Groups VII-X are not relevant to restriction practice in future applications. As such, Applicant's arguments regarding a shared special technical feature regarding the rejoinder of Groups VII-X based on a shared special technical feature are moot, and will not be addressed in specific detail.

The requirement is still deemed proper and is therefore made FINAL.

Newly submitted claims 17 and 19 are directed to an invention that is independent or distinct from the invention originally claimed for the following reasons: claims 17 and 19 do not share the same special technical feature as claim 1, as set forth in the previous restriction requirement (comparison of Groups II (to which claim 17 belongs) and III (to which claim 19 belongs) with regard to Group I), and as responded to in the arguments set forth above in relation to Applicant's traversal of the restriction requirement. Accordingly, claims 17 and 19 are withdrawn from consideration as being directed to a non-elected invention. See 37 CFR 1.142(b) and MPEP § 821.03.

Claims 1-19 are pending in the instant application. Claims 2, 6, 8-13, 17 and 19 have been withdrawn from consideration as being drawn to a non-elected invention. Claims 1, 3-5, 7, 14-16 and 18 are under examination in the instant application.

Priority

Acknowledgment is made of applicant's claim for foreign priority under 35 U.S.C. 119(a)-(d). The certified copy has been filed in this National stage application.

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However, it is noted that there is no translation accompanying the Foreign Patent document, which is presented in a language that is not English. Since no determination of priority can be made with regard to the claimed subject matter in the foreign application, the priority date of the instant application is considered to be the filing date of the International Application (June 9, 2000), until such time that a translation of the foreign document is provided and a determination of priority for the claimed subject matter can be established.

Information Disclosure Statement

The information disclosure statements filed December 10, 2001, March 18, 2002 and October 24, 2002 have been considered, and a signed and initialed copy of the form Pto-1449s have been attached to this Office Action.

Specification

The abstract of the disclosure is objected to because it recites the term "novel." This term is improper because it is presumed that all patents that issue represent "novel" embodiments. Correction is required. See MPEP § 608.01(b).

Claim Rejections - 35 USC § 101

35 U.S.C. 101 reads as follows:

Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

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Claims 1 and 7 are rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter. The claims are directed to nucleic acids as they occur in nature, which represents unpatentable subject matter. It would be remedial to indicate that the nucleic acids are "isolated" or "recombinant."

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1, 3-5, 14-16 and 18 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Applicant claims a DNA encoding a protein comprising an amino acid sequence in which one or more amino acids of SEQ ID NO: 2 or 4 "have been substituted, deleted, inserted or added, and wherein said amino acid sequence encodes a protein having the activity of binding to Reg protein." The claims read on a broad genus of DNA sequences encoding *any* protein having the capacity to bind to Reg protein because there is no limit to the number or nature of alterations that can be made to the amino acid sequence of SEQ ID NO: 2 or 4.

The written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species by actual reduction to practice or by disclosure of relevant identifying characteristics, i.e. structure or other physical

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and/or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics sufficient to show applicants were in possession of the claimed genus. In the instant case, the specification does not sufficiently describe a representative number of species by actual reduction to practice or by disclosure of relevant identifying characteristics.

Applicant claims a nucleic acid encoding an amino acid sequence in which one or more amino acids of SEQ ID NO: 2 or 4 “have been substituted, deleted, inserted or added, and wherein said amino acid sequence encodes a protein having the activity of binding to Reg protein” by function only, without any disclosed or known correlation between the elements and their function. The claims read on a nucleic acid encoding *any* protein having the ability to interact with Reg because the protein can be completely modified by any combination of additions, deletions, substitutions or insertions. The specification only provides teachings regarding DNA sequences encoding SEQ ID NO: 2 and 4, and their ability to bind to Reg. The specification does not teach how to make any protein that can bind to Reg because the specification does not disclose which sequences/domains/motifs are essential to the functional requirement of binding to Reg. In the absence of a description of what sequences/domains/motifs are required for binding to Reg, the skilled artisan cannot envision a sufficient number of embodiments of the instant invention from the instant specification because the skilled artisan can have no idea of the minimal structural requirements to achieve the claimed functions.

The prior art does not provide sufficient information on the subject to overcome the deficiencies of the instant specification. There is no description in the prior art that

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allows one to envision a representative number of amino acid sequences that can bind to Reg by disclosing structural or functional features of a Reg-binding protein so that one of skill in the art could envision the claimed invention. As such, the skilled artisan cannot envision the nucleic acids encoding such proteins. Thus the skilled artisan cannot rely on the prior art to envision a sufficient number of embodiments of the instant invention to see that the applicant was in possession of the claimed genus.

Neither the specification of the instant application or the prior art teaches a structure-function relationship for a representative number of Reg-binding proteins such that the skilled artisan can envision a nucleic acid encoding any protein that has the ability to bind to Reg. As a result, the skilled artisan would not be able to envision the claimed invention by relying on the teachings of the prior art or the instant specification. Therefore applicant has not satisfied the written description requirement to show the skilled artisan that they were in possession of the claimed genus.

Claims 1 and 3-5 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a DNA sequence encoding SEQ ID NO: 2 or SEQ ID NO: 4, or a DNA sequence of SEQ ID NO: 1 or SEQ ID NO: 3 (or sequence which hybridizes to said DNA sequences), does not reasonably provide enablement for a DNA encoding a protein comprising an amino acid sequence in which one or more amino acids of SEQ ID NO: 2 or 4 "have been substituted, deleted, inserted or added, and wherein said amino acid sequence encodes a protein having the activity of binding to Reg protein." The specification does not enable any person skilled in the art to which it

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pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

The test of enablement is whether one skilled in the art could make and use the claimed invention from the disclosures in the specification coupled with information known in the art without undue experimentation (*United States v. Telectronics*, 8 USPQ2d 1217 (Fed. Cir. 1988)). Whether undue experimentation is needed is not based upon a single factor but rather is a conclusion reached by weighing many factors. These factors were outlined in *Ex parte Forman*, 230 USPQ 546 (Bd. Pat. App. & Inter. 1986) and again in *In re Wands*, 8 USPQ2d 1400 (Fed. Cir. 1988), and the most relevant factors are indicated below:

Nature of the invention. The nature of the invention is a nucleic acid that encodes a protein that has the capacity to bind to Reg. The instant claims are directed to a nucleic acid encoding any protein with this capacity because there is no limitation as to the nature or number of alterations that can be made to the protein encoded by the claimed DNA.

Scope of the invention. The scope of the invention is broad, encompassing a nucleic acid encoding any protein that has the capacity to bind to Reg. This is because there is no limitation as to the nature or number of alterations that can be made to the protein encoded by the claimed DNA, as set forth in sections (c) and (g) of the instant claims.

State of the art. The state of the art indicates the identification of proteins having up to 97% homology to the proteins of SEQ ID NO: 2 and 4 (Van Hui *et al.*; see entire document; IDS reference; henceforth Van Hui). However, there is no identification of the domains/motifs/specific sequences within these proteins that have the capacity to bind to Reg. Indeed, even in post-filing art concerning the proteins identified herein

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(Kobayashi *et al.*; see entire document; IDS reference; henceforth Kobayashi), there is no indication of what sequences are required for the functional ability of a protein to bind to Reg. Therefore, the prior art fails to teach the necessary components of a protein that are required for binding to Reg.

In the absence of such teachings, the skilled artisan is left to determine the functional ability of a protein to bind to Reg based simply on a comparison of homology between a known protein (e.g., SEQ ID NO: 2 or 4) and a protein of unknown function. However, the state of the art indicates that basing function based solely of a comparison of homology is highly unpredictable. This was demonstrated, for example, by the conflicting publications of Scott *et al.* (*Nature Genetics* **21**: 440-443, 1999; see entire document; henceforth Scott) and Everett *et al.* (*Nature Genetics* **17**: 411-422, 1997; see entire document; henceforth Everett) regarding the cloning and characterization of PDS. Everett initially identified and sequenced the protein, predicting based upon the sequence that the PDS gene product functioned as a sulphate ion transporter protein because of its similarity to a family of known sulphate ion transporters (see for example the Abstract and page 419, right column, second full paragraph). However, further characterization done by Scott indicated that PDS was not a sulphate ion transporter because it was unable to transport sulphate ions; rather, Scott identified that PDS was a chloride and iodide ion transporter (see for example the Abstract and page 440, the paragraph bridging the left and right columns to the second full paragraph). Scott further indicated that their results underscored the importance of establishing function even in the face of significant homology to proteins of known function (see for example page 441, left column, third full paragraph), thereby establishing that function based on homology is an unpredictable

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endeavor. Therefore, the skilled artisan cannot predictably rely on sequence comparisons to determine the function of an unknown protein, as dictated by the prior art.

Because of the absence of teachings in the prior art to indicate the functional sequences required for Reg-binding activity, and because of the unpredictable nature of determining function based on homology, the skilled artisan would necessarily turn to the instant specification for guidance on how to make the broad scope of the claimed invention.

Number of working examples and Guidance provided by applicant. The instant specification does not remedy the deficiencies of the prior art. There are no teachings in the instant specification that indicate what minimal structural features of a protein are required as it regards the functional ability to bind to Reg. In the absence of such teachings, the skilled artisan cannot make the nucleic acids encoding proteins with such a function. Rather, the instant specification only provides teachings as it regards the DNA sequences that encode SEQ ID NO: 2 and 4, and the ability of these proteins to bind to Reg.

Unpredictability of the art and Amount of experimentation required. The broad scope of the claimed invention is highly unpredictable in view of the teachings of the prior art and the instant specification. While the prior art discloses a sequence that is 97% homologous to SEQ ID NO: 2 and 4 of the instant specification, there is no functional characterization of the protein to determine what portions or minimal sequences of the protein are required to achieve the claimed functional limitation of binding to Reg. Furthermore, the skilled artisan cannot rely simply on sequence homology to ascertain the functional ability of a protein because, as taught by Scott in

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view of Everett, doing so is highly unpredictable. Finally, the instant specification provides no guidance on the minimal sequence requirements for binding to Reg. In the absence of these teachings, the skilled artisan would be required to practice an empirical procedure of trial and error experimentation to discern which proteins and protein variants (besides SEQ ID NO: 2 and 4) have the capacity to bind to Reg. Thus, the broad scope of the claims merely represents an invitation to experimentally determine what proteins and protein variants are capable of binding to Reg (i.e., what proteins are claimed in the instant invention), and what corresponding nucleic acids encode such proteins.

In conclusion, although the instant claims read on a nucleic acid encoding any protein having the capacity to bind to Reg, the teachings of the prior art and the instant specification fail to give substantial guidance in the making and using of the broadly claimed genus of nucleic acids. In the absence of such guidance, the broad scope of the claims is not enabled.

Claims 14-16 and 18 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The test of enablement is whether one skilled in the art could make and use the claimed invention from the disclosures in the specification coupled with information known in the art without undue experimentation (*United States v. Telectronics*, 8 USPQ2d 1217 (Fed. Cir. 1988)). Whether undue experimentation is needed is not based

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upon a single factor but rather is a conclusion reached by weighing many factors. These factors were outlined in *Ex parte Forman*, 230 USPQ 546 (Bd. Pat. App. & Inter. 1986) and again in *In re Wands*, 8 USPQ2d 1400 (Fed. Cir. 1988), and the most relevant factors are indicated below:

Nature of the invention. The nature of the invention is a pharmaceutical composition comprising a nucleic acid. The characterization of the composition as being “pharmaceutical” attaches a moniker of “gene therapy” to the claimed invention. Therefore, the instant claims read on a composition where the use of the composition is for gene therapy.

In addition, the claims also are directed to a nucleic acid encoding any protein with this capacity (and pharmaceutical compositions thereof) because there is no limitation as to the nature or number of alterations that can be made to the protein encoded by the claimed DNA. Thus, the same considerations set forth above for claims 1 and 3-5, as it regards the nature of the nucleic acid encoding the protein, are applicable to claims 14-16 and 18.

Scope of the invention. The scope of the invention is broad, encompassing a nucleic acid encoding any protein that has the capacity to bind to Reg ,and its use as a pharmaceutical composition. This is because there is no limitation as to the nature or number of alterations that can be made to the protein encoded by the claimed DNA, as set forth in sections (c) and (g) of the instant claims.

State of the art and Level of skill in the art. The State of the art as it regards techniques for gene therapy is highly unpredictable. In a review from 1997, Verma *et al.* (*Nature* 389:239-242, 1997; see entire document) asserted that there were conceptual

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hurdles that needed to be addressed prior to gene therapy becoming a routine practice (see for example page 239, left column, second paragraph). The primary deficiencies of gene therapy are the ability to sufficiently deliver a gene to the proper location, and then maintain the expression of that gene at a therapeutic level (see for example page 239, right column, first full paragraph). In a separate review by Anderson (*Nature* 392:26-30, 1998; see entire document), it was reiterated that several problems existed with regard to the predictable practice of gene therapy techniques, including efficient delivery and sustaining sufficient expression of the gene (see for example page 26, right column, first full paragraph). Finally, it was recently reported that, in what was considered gene therapy's only true success (Erika Check *Nature* 421:305; see entire document), the targeting of the gene therapy vector was found to improperly integrate, causing childhood leukemia in some of the patients that were treated. These references teach that performing gene therapy is at best unpredictable.

In addition to the unpredictability associated with gene therapy, there is also the unpredictability associated with making a nucleic acid encoding any protein that has the capacity to bind to Reg, as set forth above in the rejection of claims 1 and 3-5. To briefly reiterate, there is no identification of the domains/motifs/specific sequences within these proteins that have the capacity to bind to Reg, even in post-filing art. Therefore the skilled artisan would be at a loss to make the broad scope of nucleic acids that encode any protein having the capacity to bind to Reg. Furthermore, the skilled artisan could not rely on a simple homology comparison to determine these sequences because, as established in the prior art regarding the conflicting reports of Everett and Scott (see

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rejection of claims 1 and 3-5 above for a complete analysis), predicting function based upon sequence homology alone is unpredictable at best.

Because of the unpredictability associated with gene therapy that is prevalent in the State of the art, in addition to the absence of teachings in the prior art to indicate the functional sequences required for Reg-binding activity and the unpredictable nature of determining function based on homology, the skilled artisan would necessarily turn to the instant specification for guidance on how to make the claimed invention involving gene therapy pharmaceuticals.

Number of working examples and Guidance provided by applicant. The instant specification provides no details of using the instantly claimed nucleic acids as pharmaceutical compositions (i.e., in gene therapy). The instant specification does not teach how to overcome the deficiencies of gene therapy as a whole, namely the ability to sufficiently deliver a gene to a cell (without developing an alternative condition, such as leukemia) and, upon delivery, the ability to express the nucleic acid at therapeutically enabling amounts. In essence, the instant specification provides no enabled therapeutic use for the nucleic acids, therefore the pharmaceutical compositions are not enabled.

Additionally, the instant specification only provides teachings as it regards the DNA sequences that encode SEQ ID NO: 2 and 4, and the ability of these proteins to bind to Reg. Therefore, even beyond the context of the instantly claimed pharmaceutical compositions, the claims lack enablement for the broad scope of nucleic acids that are included within the pharmaceutical compositions.

Unpredictability of the art and Amount of experimentation required. The art of gene therapy is highly unpredictable, as established by the teachings set forth in the discussion

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of the State of the art. As per the teachings of the prior art, in order for the instant specification to enable a pharmaceutical composition comprising nucleic acids, the instant specification would be required to teach how to overcome the deficiencies set forth in the prior art (appropriate delivery and expression of the desired nucleic acid). However, there are no teachings in the instant specification to establish that the employment of gene therapy is routine. Thus one of skill in the art must defer to the teachings of the prior art, which indicates the unpredictability of gene therapy. As such, in order to use the claimed invention, the skilled artisan would have to empirically determine how to sufficiently target and express the nucleic acids within the pharmaceutical compositions in a therapeutic context. This represents an invitation to undue and unpredictable trial and error experimentation, especially in light of the fact that, over the past 7 years (at least), no one has been able to establish a routine gene therapy protocol.

In addition to the unpredictable nature of the compositions as they relate to gene therapy, the compositions have the added element of unpredictability associated with determining which nucleic acids encode proteins and protein variants (besides SEQ ID NO: 2 and 4) that have the capacity to bind to Reg. As established above (and in the rejection of claims 1 and 3-5, explicitly), the broad scope of the claimed invention is highly unpredictable in view of the teachings of the prior art and the instant specification because there is no teaching regarding the domains/motifs/specific sequences that have the functional capacity to bind to Reg. The skilled artisan cannot rely simply on sequence homology to ascertain the functional ability of a protein because, and the instant specification provides no guidance on the minimal sequence requirements for binding to

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Reg. In the absence of these teachings, the skilled artisan would be required to practice an empirical procedure of trial and error experimentation to discern which nucleic acids encode proteins and protein variants (besides SEQ ID NO: 2 and 4) that have the capacity to bind to Reg. Thus, the broad scope of the claims merely represents an invitation to experimentally determine what proteins and protein variants are capable of binding to Reg (i.e., what proteins are claimed in the instant invention), and what corresponding nucleic acids encode such proteins.

In light of the highly unpredictable nature of gene therapy (i.e., the therapeutic connotation placed on the pharmaceutical compositions as claimed), in addition to the unpredictability associated with the broad scope of the nucleic acids encoding the proteins that is claimed, the instant claims are not enabled.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Prior to setting forth the grounds of rejection, the examiner wishes to clarify that the pharmaceutical compositions are also anticipated by the instant reference because the only limitation set forth in the claim is that it comprises the DNA of claim 1. Therefore, the compositions are anticipated although the intended use (gene therapy, as a pharmaceutical composition) is not enabled.

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Claims 1, 7 and 14-16 are rejected under 35 U.S.C. 102(b) as being anticipated by Van Hui *et al.* (IDS reference; see entire document; henceforth Van Hui).

Van Hui teaches the identification a DNA sequence that encodes a protein that has 97% homology to SEQ ID NO: 2 and 4, which falls well within the limitation in which one or more amino acids of SEQ ID NO: 2 or 4 “have been substituted, deleted, inserted or added, and wherein said amino acid sequence encodes a protein having the activity of binding to Reg protein.” Absent evidence to the contrary, and due to the high homology of the two proteins, the protein disclosed by Van Hui has the inherent ability to bind to Reg (and thus, the indicated limitations set forth in the pharmaceutical claim 15). Additionally, absent any evidence to the contrary, the DNA sequence disclosed by Van Hui will have the capacity to hybridize to either SEQ ID NO: 1 or 3. As such, Van Hui teaches each and every aspect of the claims identified in the rejection.

Allowable Subject Matter

No claims are allowable.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to David A. Lambertson whose telephone number is (571) 272-0771. The examiner can normally be reached on 6:30am to 4pm, Mon.-Fri., first Friday off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Remy Yucel, Ph.D. can be reached on (571) 272-0781. The fax phone

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number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

David A. Lambertson, Ph.D.
AU 1636



JAMES KETTER
PRIMARY EXAMINER